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THE AMERICAN
JOURNAL OF PHARMACY

VOL. 101 DECEMBER, 1929 NO. 12

EDITORIAL

SO SIMPLE A DEVICE AS THE THERMOMETER

INVENTION rarely becomes full-blown like "Jove begat Minerva" but slowly, as growth comes to a crystal.

Molecules, swayed by a naive, attractive nucleus, slowly gather to their work—each contributing its share—each going to its appointed place, somewhere in the pattern.

The dross is left without, and only the pure and the belonging find room in the form of the finished crystal.

So, too, it seems with all inventions. A thousand minds contribute—at a thousand odd intervals—and finally—out of the incoherent whole emerges the needed invention.

Witness the evolution of so simple a device as the thermometer.

A crude instrument for determining temperature is said to have been devised by Galileo in 1593. Sanctorious first used it in the diagnosis of fevers in 1611, and an old illustration of this early instrument makes it appear more like a saxophone than a thermometer. Leucheron in 1624, baptized the instrument with the name which it still carries.

The first graded thermometer was made by Ferdinand II, Grand Duke of Tuscany, in 1641. He used a movable scale.

The first thermometer with a fixed scale was made by Fabri, in 1661, using snow for the low point and midsummer heat for the high.

In 1664, Robert Hooke proposed the freezing point of water as the low fixed point, and, in 1665, he drew specifications for the manufacture and graduation of comparable spirit thermometers with the freezing point of water as the zero of their scales, and he evidently recognized it as fixed.

Halley, in 1693, stated that the temperature of boiling water is constant—much more constant than a comet's tail. This fact was proven by Amontons, in 1702.

In 1701, Sir Isaac Newton proposed a thermometer scale with the freezing point of water as zero and the temperature of the human body as 12 degrees.

Fahrenheit, in 1714, introduced a thermometer, using spirit of wine as the expanding medium, and taking, as fixed points, the temperature of the human body and that of a mixture of ice and common salt. In 1721, he made a mercury thermometer, according to Halley's suggestion, of 1693, and, in experiments with this instrument, he proved the dependence of the boiling point upon pressure.

In 1731, Reaumur devised his scale, which uses zero as the freezing point and 80 degrees above as the boiling point. This scale has been quite generally used in Europe until recently. At the present time, it is used chiefly in breweries, in Europe, too, of course.

In 1742, Celcius devised a scale in which he used the melting point of ice as 100 degrees and the boiling point of water, as the zero point.

The next year, 1743, Christian introduced this scale inverted, using zero for the melting point of ice and 100 degrees as the boiling point of water. This is the Centigrade scale in common use.

The next important step was made by Currie of Liverpool, who published his investigations under the title of "Medical Reports on the effect of Water, cold and warm, as a Remedy in Fever and other diseases" in 1797. The whole of his observations were based on thermometry, and he made careful records of the temperatures in his case histories. Currie's work, though it attracted little attention at the time, is remarkable, and is now historic, as he thus undoubtedly laid the foundations of modern clinical thermometry.

It is interesting here to note, that Dr. Archibald Arnott, who was one of the physicians in charge of Napoleon Bonaparte, took the temperature of the ex-emperor on April 3, 1821, when he was taken ill at St. Helena. Like Currie, he was a graduate of Edinburgh. In 1840, William Arnold, another Scottish physician, devoted a chapter in his book on the "Temperature of the System," to the use of the thermometer in disease, and notes that he took his temperatures under the tongue and in the axilla.

Aikin's thermometers which he used in the English Hospital in 1865-67 were looked upon as novelties, being ten inches long

and taking five minutes to record the temperature. The present short thermometer dates from 1867 being devised by Clifford Allbutt.

Since then no radical change has been made.

And so it is seen that the trail of a device, even so simple as a thermometer, is a long, long trail indeed—and that the really important ingredients of every human accomplishment are patience and perseverance.

IVOR GRIFFITH.

ORIGINAL ARTICLES

LICORICE*

By John Uri Lloyd, Cincinnati, Ohio.

HISTORY.—The licorice plant abounds over an extensive area of the warm portions of Europe, including some of the Mediterranean islands, thence into Asia, where it is abundant in great sections of Turkey and Persia. Many varieties are recognized by botanists, but the drug of commerce is yielded by two principal varieties of Glycyrrhiza glabra, recognized as official. The plant has been known and used from antiquity to the present time.

Theophrastus refers to a sweet Scythian root, growing near the lake, Maeotis (Sea of Azov), used in cough and pectoral affections. Dioscorides gives it a place, describing two varieties of the plant, while the Roman writers, Celsus and Scribonius Largus, call it the *sweet root, Radix Dulcis.* Pliny, of course, met it in the sections about his own country, and describes it as native to Cilicia.

Not only does licorice grow wild throughout large sections of the world, but is also cultivated. However, it is so abundant in its native land, where labor is cheap, as to render its cultivation in most other sections unprofitable.

There can be no more aggressive weed in any locality than is the licorice plant in the rich bottom lands of Turkey. Immense

*My thanks are due to Professor Thomas H. Norton for introducing me to the manufacturers and dealers in licorice in and about Smyrna. Credit for information relative to manipulation, as well as statistics, is due to Marenti & Co., Smyrna, and MacAndrews & Forbes, Sokia. The accompanying photographs were also taken by me in the licorice industries of these firms. Paper was written from notes of my travels, 1906.

amounts of the drug are exported from Smyrna and large quantities of licorice extract (paste) are made in both Smyrna and Sokia. Having made a study of licorice in its homeland, where it has existed from time immemorial, I shall limit my remarks to conditions that exist there.

The history of Smyrna licorice is briefly given as follows: Over half a century ago, a traveler recently returned from Turkey, in a lecture before a London audience, referred to the enormous growth of licorice in the valleys of the Meander and Hermus in Asia Minor. This came to the attention of the MacAndrews, a Scotch firm of ship owners whose steamers were engaged in carrying licorice, licorice paste, oranges, etc., from Spain. MacAndrews sent a man named

Ploughboy in the Licorice Valley of the Hermus

Clark (whose wife still lived near Smyrna in 1906) to investigate. He found a native (Graeco-Italian) pasteworks operating at Cutzarlee. Mr. Clark gave a most favorable report to his employers, who started a factory at Sokia, across the Meander valley from Cutzarlee. The root was so abundant and labor so cheap that it cost but one-tenth the price the Spaniards and Italians paid in their countries. Consequently, the profits were enormous, and from this beginning, which has made great fortunes for the investors, the licorice industry of Turkey has developed.

Description.—The licorice plant prefers the richest land and covers vast areas of the bottoms about the rivers, Hermus and Meander. It not only covers the valleys, but creeps up the hillsides. The

rich meadows about the ancient cities of Priene and Magnesia are threaded with licorice. It wedges itself between the stones of the ancient roadway of the Greeks. The wheat fields of the adjacent valley are no sooner plowed than its bean-like vine heads appear. The stones of the mountain slopes collect earth which also harbors the weed, for in this country licorice is a weed that cannot be exterminated. Naturally, only soft earth can yield a profitable return to the digger.

Fragments of Greek or Roman Ruins in Valley of the Hermus. Origin Unknown

In the licorice lands every crop has licorice as a companion. It is probable that this has been the case throughout the period that marked the rise and fall of empires and of recurringly destroyed and ever-crumbling cities, such as Ephesus and Priene, whose rich valleys have been cultivated from the beginning of history, and are yet so fertile as to make one question the possibility of their exhaustion. In this home of marvelous fertility the licorice plant is master. Yet it is a kindly master, for in these very fields are grown such crops of wheat, such vegetables and fruit as to astound one who con-

templates the fact that since the days of antiquity these fields have, without fertilization, fed hordes of Roman, Greek, Turkish and other nations, as empires successively rose and fell. In fields about the river Meander, thickly threaded with licorice, near the ancient city of Priene, I stood in wheat which thick as grass, rose above my head.*

Valley of the Hermus River. Licorice Digger in the Foreground. Turkish Graveyard Marked by Cypress Trees in Background

Gathering Licorice.—In the fall the plant dies to the ground, but the root lives over the winter. The undried stem stalk is often the size of the wrist, or even larger. From its crown dips a root that runs down, in accordance with the soil, from two to even five or six feet. From this tap root radiate horizontal branches that extend

*I can but question if the leguminous plant, licorice, may not have the power of harboring colonies of bacteria to fix atmospheric nitrogen as a food. This, it seems to me, needs to be investigated.

several feet outward. All parts of the underground portion are marketable.

The Licorice Digger.—From the station, Sokia, and other licorice centers in the licorice season one may see at daybreak the native diggers, mounted on donkeys, striking out into the valley of the Meander. They ride from six to eight miles to suitable locations and begin their task. A heavy grubbing hoe is employed. The digging of each tap root requires the sinking of a pit in the earth from which deep furrows must be dug to procure the radiating side roots.

Licorice Stacks Near Wreckage of Old Roman Highway

As the diggers proceed the earth behind them is thus cast into uneven hillocks and trenches. At nine o'clock the lunch of bread and a bit of sweet cheese, perhaps a few olives or a little molasses, is eaten. Never any wine in this land of grapes and wine, for to Turkish people wine or other alcoholic drink is forbidden by decree of the Koran. Again they patiently work until evening, partaking of no midday meal. Finally the day's product is loaded on the donkey, and, when the distant station is reached, weighed and paid for. The maximum of a day's yield is fifty cents; sometimes it is as low as

Turks Digging Licorice. Old Roman Roadway in Background

Nine O'Clock Lunch, in Which Author Joined

Licorice, Dried, Being Turned Over

Primitive Methods of Transferring Licorice

twenty cents. Out of this the laborer lives, furnishes and feeds the donkey and supports his family.

A field in the valley of the historic Meander, dotted with licorice diggers and their donkeys, is picturesque in the extreme.

The digger does not exterminate the plant. The runners are furnished with buds, and all the root fragments left in the ground throw up new sprouts. In three or four years the same earth is again ready for the grubbing hoe, the patient Turk is again ready for his task. Should the ground be cropped in the meantime, the licorice still thrives, a live and let-live weed.

The Root.—The licorice root is dirty brown and very scraggly. It makes a tortuous, unsightly heap when piled by the diggers in good-size heaps. These stacks are forked over into new locations from four to six times. Especially is this necessary during damp weather. When dry, the root is thrown into great heaps, thousands of pounds each, and, if possible, roofed over or covered with canvas.

Manipulation.—The root is now transferred to the factory and either ground coarsely and extracted or baled by pressure and exported to America, where the customs' duty prevents the profitable entrance of extract. For pharmaceutical purposes and in other directions where nice appearing root is preferred, the heaps are sorted by girls, women and boys, who select the long straight roots and cut them into proper lengths. These are sorted and wired into large bundles, to be re-bundled into smaller bundles in the country of their destination. The women earn from twenty to thirty cents a day, but are diligent and happy. In the station near Magnesia I observed twenty-five or thirty women sorting the root, but in Sokia saw only extract manipulation and baling for American export.

Taking it all in all, the Turkish licorice industry, so far as the drug is concerned, consists simply in the collecting of a wild root that grows in lavish abundance over an immense area of Asia Minor. It gives employment to a small army of very poor peasants, who, by hard labor, exist in the most frugal manner.

There seems no probability of the exhaustion of this industry, notwithstanding the immense amounts demanded for export and consumed in the making of licorice paste to be used in the European and American tobacco industries.

Licorice Extract.—This is known as licorice paste, and is made in the most primitive manner. The drug is coarsely ground and mixed with water in iron or copper tanks and is then boiled. The

Woman Sorting Licorice

Baling Licorice for Export

decoction is drawn off, the dregs again covered and boiled as before. The dregs are then squeezed by hydraulic pressure. The decoctions are mixed and boiled in tanks until reduced to the consistency of tar, then carefully concentrated over a slow heat to a thick, black magma. This is drawn off and poured hot into paper-lined wooden boxes. These boxes hold about three hundred pounds of the paste, which, when finished, contains 25 to 26 per cent. moisture. The root produces from 40 to even 50 per cent. of its weight of paste. To concentrate beyond this point without a vacuum apparatus injures the

Boys Peeling Licorice

product by reason of the high temperature. The use of the vacuum, which reduces the moisture to 20 per cent., is a feature of some establishments.

Licorice paste is of a dark—nearly black—color, has a slightly licorice odor and a lingering, intensely sweet taste. It is largely soluble in water, and especially so in alkaline saliva. The paste made in Turkey is mostly exported to European countries, where it is used mainly in the tobacco industry. The American duty on the extract necessitates the exportation of the crude drug to America, where the paste is then manufactured. In questioning the extract makers

I was told that glycyrrhizin did not answer the purpose of the extract. It did not carry the full sweeting qualities nor did it possess the flavor of the drug. Its manufacture had, therefore, been abandoned in favor of the established process of licorice extract.

Statistics.—Smyrna is the principal port of export for both licorice root and paste. The American Tobacco Trust controls the larger acreage of licorice land in the vicinity of Smyrna, and also in other sections of Asia Minor. Its aggressiveness has largely resulted in the destruction of the business of the licorice dealers who formerly supplied the drug and its extract.

Licorice paste contains 25 per cent. moisture.

Root yields 40 per cent. paste.

Paste yields 21 or 22 per cent. glycyrrhizin.

Sells at thirty-four shillings for 112 pounds delivered at Liverpool.

Men dig one hundred pounds per day.

Diggers' wages, twenty-five to thirty cents.

Lost in drying, 50 per cent.

EXPERIMENTS WITH EXTRACTS FROM THE WOOLLY-POD MILKWEED (Asclepias eriocarpa)

By James Fitton Couch

Pathological Division, Bureau of Animal Industry, Washington, D. C.

THE WOOLLY-POD MILKWEED, *Asclepias eriocarpa* Benth., has been recognized for some forty years as a poisonous plant (2). Up to the present, however, there has been no reported chemical examination of it. Such a study was undertaken as a part of the investigations made in this laboratory on the poisonous species of the genus *Asclepias* and certain definite results were obtained which are reported in this paper.

The material used consisted of dried whole plant collected in Fresno County, California. A total of 15.6 kg. of the plant was used. The general methods employed were similar to those that have been in use in this laboratory for some time and which have been previously described at length. (1) A preliminary experiment indicated that the toxic constituent was completely extracted from the plant by hot water, consequently the main portion was exhausted with that

solvent, the water extract was fractionated, and the various fractions tested for toxicity on guinea pigs and sheep. The diagram illustrates the method of fractionation and the designations of the fractions obtained. The pharmacological experiments are summarized in Table 1.

Fraction B. The Marc

Two ounces of ground dried leaves equivalent to 0.5 pound of green leaves were thoroughly extracted by several portions of boiling water. The residual marc was force-fed to sheep 672 and did not affect the animal. The amount given was at least twice the lethal dose and the experiment indicated that the treatment with water had either decomposed the toxic substance or had dissolved it out of the plant tissue.

Fraction A. The Water Extract

The water extract from the main portion of the material was a dark-brown cloudy mass of disagreeable putrefactive odor. It produced minute precipitates with alkaloidal reagents, reduced alkaline copper solution, produced a flocculent precipitate with phenylhydrazine and a heavy precipitate with barium-hydroxide solution. A portion of the water extract was given to guinea pig No. 210 by mouth, the dose being small but not accurately known. In an hour the animal was exhibiting symptoms of severe depression. The respiration, at first very rapid, became dyspneic. The symptoms became more pronounced and the animal died on the third day. The postmortem examination revealed nothing of an abnormal nature.

A quantity of the water extract equal to 7.77 kg. of dried plant was dissolved in water and thoroughly precipitated by saturated solution of barium hydroxide in excess. The bulky precipitate was filtered off and washed with the precipitant. The precipitate was designated fraction AA and the filtrate AB.

Fraction AB. Not Precipitated by Barium

The fraction was freed from barium by the addition of sodium bicarbonate and removal of the last traces with sodium sulphate. 50 cc. of the final liquor was evaporated to dryness, ashed, and the ash was tested for barium. None was found. Two doses of this fraction were given to guinea pig 211 without effect. Three doses were

given to sheep 782; on May 22 the sheep received a drench containing the equivalent of 45.4 gm. of plant, on the following day the dose was doubled and on May 24 the sheep received four times the original dose without effect. The total dose was equivalent to 317.8 gm. of dried plant or 334.5 grams per hundredweight of sheep. Since this dose was at least ten times the lethal dose of the plant it was evident that the barium treatment had removed the toxic substance from solution.

Fraction AA. The Barium Precipitate

A test portion of the barium precipitate was extracted thoroughly with alcohol. The solvent was removed and the residue, after barium was proved absent, was taken up in a little water and drenched into guinea pig 224. There was no effect from this dose. Inasmuch as the toxic substance is now known to be soluble in alcohol it is evident from this feeding that it was in chemical combination with barium in the precipitate.

Since there was some evidence that the toxic substance might be a saponin this possibility was investigated. The whole barium precipitate was treated with several portions of boiling water and the solutions were filtered, freed from barium with sodium sulphate, and concentrated. The fraction was designated AAB. It reduced alkaline copper solutions only after hydrolysis with mineral acid and then very slightly. It gave a slight test for alkaloids, formed a small and non-persistent froth, and did not hemolyze washed sheep's corpuscles. Five cc. of the concentrate equivalent to 103.5 grams of dried plant per hundredweight of sheep were given by mouth to sheep 782 on June 2, and produced no effect.

Fraction AAC

The residue of barium precipitate insoluble in water was now suspended in water and decomposed by sulphuric acid in slight excess. The precipitate was filtered off and the filtrate, after neutralization with sodium carbonate, was concentrated to small volume and tested as fraction AAC.

On August 8, sheep 782 received by mouth a dose of 10 cc. of the extract equivalent to 88.4 grams of dried plant per hundredweight. There was no effect and the dose was repeated on the fol-

lowing day. The animal was kept under observation for a week and showed nothing abnormal. Then four times the original dose was given, or 353.6 grams per hundredweight. There was no effect from this dose. The total dose was 530.4 grams per hundredweight or at least seventeen times the lethal dose.

Fraction AAD

The precipitated barium sulphate from which fraction AAC was filtered was suspended in 1 per cent. sodium-carbonate solution in order to dissolve possible acidic compounds, insoluble in water, that might be present. The alkaline solution did extract a soluble material from the precipitate. The solution was filtered and the filtrate was evaporated to a small volume. It was bottled and preserved. After standing some weeks it developed a disgusting ammoniacal odor resembling that observed when the plant extract was being concentrated.

A solution of the fraction was given by mouth to two guinea pigs. No. 276 received the equivalent of 10 gm. of dried plant and No. 271 the equivalent of 5 gm. No. 276 died in 24 hours; No. 271 was sick but recovered.

A larger quantity of this fraction was then prepared from the original water extract by the following process. A quantity of the water extract equivalent to 6.77 kg. of the dried plant was dissolved in 5 liters of water and completely precipitated with hydrochloric acid. The precipitate was collected on a filter, redissolved in sodium carbonate, reprecipitated with hydrochloric acid, washed and dried. The product was mixed with the remainder of the first lot of AAD.

Attempted Purification of AAD

The collected sample of AAD was a water-insoluble black mass of resinous fracture. It was not easily soluble in strong alcohol but dissolved readily in 75 per cent. alcohol. It did not crystallize when its solutions were allowed to evaporate. Boiling with animal charcoal failed to decolorize it. Submitted to dialysis it passed through a parchment dialyzer and the dialysate was as highly colored as the original solution. It did not reduce alkaline copper solution even after hydrolysis for several hours and its solution was not hemolytic when tested on washed sheep's corpuscles. The fraction was finally extracted thoroughly with boiling alcohol and the insoluble matters

(fraction AADB) were filtered off. The soluble fraction (AADA) was recovered by evaporating the solvent.

Fraction AADB

This fraction was a black friable, amorphous powder, insoluble in water and soluble in aqueous alkalis. A portion was dissolved in sodium-carbonate solution and given in 0.2 gm. doses to guinea pigs 279 and 280. Neither animal showed any effect from the dose.

Fraction AADA

The dried fraction weighed 19.94 gm. and represented approximately 0.3 per cent. of the original plant. A portion was dissolved in enough dilute ammonia and boiled to drive off the excess of ammonia. Doses of this solution calculated to contain 30 mg. representing 10 gm. of plant were injected intraperitoneally into guinea pigs 279 and 280. No. 279 died during the following night and 280 died on the following day after showing symptoms of depression similar to those observed with other toxic fractions. It appears from the evidence that this fraction contains the toxic constituent of *Asclepias eriocarpa*. The physical and chemical properties of the substance distinguish it sharply from the toxic constituents of *Asclepias galioides*. The principal toxic constituent of that plant is a resinous substance of the picrotoxin group and is insoluble in aqueous alkalis and very soluble in organic solvents with the exception of petroleum ether. The minor toxic constituents of the plant named are glucosides and they are moderately soluble in water.

The toxic constituent of *A. eriocarpa* differs also from that of *A. vincetoxicum* as reported by Masson [3] who found in the latter plant a substance which he named asclepiic acid which was precipitated by barium hydroxide and lead acetate and was insoluble in water but soluble in ether and chloroform as well as in aqueous alkalis. The "vincetoxine" reported by Tanret [4] also differs in physical and chemical properties from the *A. eriocarpa* poison. Tanret's substance was glucosidal and could be resolved into two components, one of which was soluble in water and the other in ether.

Summary

The woolly-pod milkweed, *Asclepias eriocarpa*, which is a dangerously poisonous plant contains a single toxic constituent. This sub-

stance is a complex organic acid, insoluble in water, acids, chloroform, and ether; soluble in aqueous alkalis and in alcohol. It has been obtained sufficiently pure to permit certain of its properties to be determined: it is non-glucosidal, non-hemolytic, does not contain basic nitrogen, and may be dialyzed.

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TABLE 1

SUMMARY OF PHARMACOLOGICAL EXPERIMENTS ON SHEEP AND GUINEA PIGS

Date	Animal	No.	Fraction fed	Dose	Plant equivalent	Effect	Termination
1922							
July 8	Sheep	672	B	2 oz.	2 oz.	None	Survival
1923							
Feb. 10	Guinea pig	210	A	4 cc.		Sick	Death
" 17	" "	211	AB	2 cc.	10 gm.	None	Survival
" 20	" "	212	AA	3 cc.	10 gm.	Sick	Death
" 28	" "	211	AB	4 cc.	20 gm.	None	Survival
Mar. 12	" "	224	AAA	4 cc.	10 gm.	None	"
1924							
May 22	Sheep	782	AB	10 cc.	45.4 gm.	None	"
" 23	"	782	AB	20 cc.	90.8 gm.	None	"
" 24	"	782	AB	40 cc.	181.6 gm.	None	"
June 2	"	782	AAB	5 cc.	98.35 gm.	None	"
Aug. 8	"	782	AAC	10 cc.	84 gm.	None	"
" 9	"	782	AAC	10 cc.	84 gm.	None	"
" 18	"	782	AAC	40 cc.	336 gm.	None	"
Nov. 8	Guinea pig	271	AAD	1 cc.	5 gm.	Sick	Recovery
" 8	" "	276	AAD	2 cc.	10 gm.	Sick	Death
1925							
Mar. 10	" "	279	AADB	0.2 gm.	100 gm.	None	Survival
" 10	" "	280	AADB	0.2 gm.	100 gm.	None	"
" 19	" "	279	AADA	0.03 gm.	10 gm.	Sick	Death
" 19	" "	280	AADA	0.03 gm.	10 gm.	Sick	Death

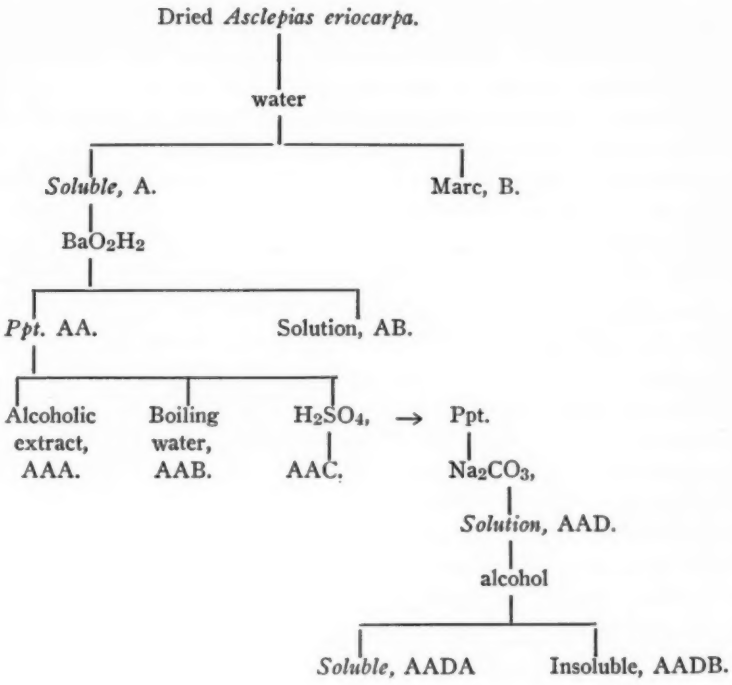

Diagram illustrating method of fractionating the aqueous extract. The active fractions are italicized.

MICROCHEMICAL BEHAVIOR OF THE OFFICIAL ALKALOIDS

By L. Rosenthaler

Communication from the Pharmaceutic Institute of the University of Berne

NOTHING IS MORE characteristic of the conservative tendency of the German Pharmacopœia, 6th edition, than the complete omission of microchemical reactions for qualitative testing of drugs. And still the thought to use microchemical reactions is not at all new. I am certain, that I was the first who publicly announced the use of these reactions (1906). During the war, I pointed out in an article, written at the front, entitled "Pharmacopœia and Economy,"

the value of microchemistry, as the general impoverishment after the war required the utmost economy. "Only microchemistry affords the economy absolutely essential from a scientific point of view at such time." That is what I wrote then, but without being able to convince leading men of the truth of my statements, if indeed they read my article. It should not be difficult to understand the enormous amount of waste, from the point of view of the microchemist, that the continuation of macrochemical methods means. To illustrate, think how much silver nitrate is wasted every day in the German pharmacies, because the German Pharmacopœia, 6th edition, specifies for the reactions of Cl a 5 per cent. silver nitrate solution, whereby each time about 0.5 cc., equal to 0.025 gm. of silver nitrate, are used, while the same and even more can be done, if the reaction is carried out with 0.005 cc. of a 1 per cent. silver nitrate solution, therefore with 0.05 mgm. of silver nitrate. What is true of the reagents, is also true of the substances to be tested, which very often are very precious. The economy of time, which as we all know means money, is considerable, also the economy of vessels and tools is considerable, as most reactions can be carried out on glass slides, often without cover glass, a few glass rods and capillary tubes being all that is necessary. Further economy can be obtained if the number of reactions is greatly restricted. In the case of organic substances, usually the determination of the melting point and one identity reaction are sufficient, and also the tests for purity can be greatly restricted, as the melting point alone indicates the presence of impurities. The pharmacopœias contain more identity and test reactions than are absolutely necessary. That is why the chemical articles in the pharmacopœias as well as the pharmacognostic articles have grown to such an extent, that a sort of a "hypertrophy" of pharmacopœias has resulted, which is particularly pronounced in the 6th edition of the German Pharmacopœia.

A field in which the superiority of the microchemical tests is particularly obvious, is that of the alkaloids. On account of the high cost of the alkaloids, the economy is self-evident. There is hardly one alkaloid which cannot be tested for all necessary qualitative and identity tests with about 2 mg. of the substance. Besides the microchemical reactions are more characteristic than those of the pharmacopœia. For instance, the German Pharmacopœia specifies four reactions for morphine, while microchemically one reaction is sufficient.

Furthermore, one has to bear in mind, that many reactions of the pharmacopœia are group reactions, for instance the formaldehyde-sulphuric acid reaction for morphine, the murexide reaction for caffeine, and many others. This does not mean that there are no group reactions in microchemical tests. In the following part the reactions described are carried out so that a tiny grain of the substance on a cover glass is dissolved in one drop of water and then one drop of the reagent added. If the reagent is a solid substance, it is added in solid form.

The test for the anions will not be mentioned each time; it is carried out as follows, even on a cover glass: Cl' is tested as already mentioned with a 1 per cent. silver nitrate solution; SO_4'' with 1 per cent. barium nitrate solution or with solid calcium acetate giving calcium sulphate; PO_4''' is tested (for instance, in codeine phosphate) with magnesia mixture as magnesium ammonium phosphate; and NO_3' is tested by means of nitron (characteristic aggregates of needles of nitron nitrate). The smallest particles of bromides will give the Schering's reaction. With sulphuric acid containing copper sulphate, a black purple precipitate.

Descriptions and illustrations will only show the main forms of crystals which are obtained. It would go entirely too far to describe in detail, everything that can be found in microchemical investigations. Colors of crystals are not mentioned. They are colorless if the components are colorless; if the components are colored, crystals are also.

Ethyl morphine hydrochloride. With ammonium thiocyanate, prisms, thin rods, spear-shaped crystals or needles, partly curved, single or in larger aggregates. Sodium hydroxide produces permanent turbidity, ammonia, on stirring a transient one. A mixture of starch and a 1 per cent. solution of iodic acid should not give, on the addition of ethylmorphine hydrochloride, a blue coloration of the starch granules.

Alypine hydrochloride, with ammonium thiocyanate at once or soon a formation of aggregates of needles or rods; with potassium iodide immediate aggregates of partly curved and partly branched needles. With Reinecke's salt either single or aggregated needles are obtained. With 3 per cent. chromic acid, a turbidity (in droplets) is formed, soluble in 10 per cent. hydrochloric acid. (Distinction from cocaine.)

Alypine nitrate gives all the above reactions.

Apomorphine hydrochloride. With potassium bromide promptly crystals separate. These are simple prismatic crystals. With 1 per cent. mercuric acetate solution, yellow grains of apomorphine hydrochloride will gradually become reddish to greenish; on evaporation of the solution, the margin turns green, and green, bush-like forms are obtained. With iodic acid, deep brown-red is obtained with liberation of iodine, detected by odor or starch. The aqueous solution gives with sodium hydroxide, at the contact zone, a turbidity, which goes into solution on stirring, Soon, however, the formation of insoluble particles occurs, with discoloration of the entire solution.

Arecoline: hydrobromide. With Reinecke's salt, at once the formation of aggregates of small, later larger, needles. If a grain of acroleine hydrobromide is dropped into one drop of 5 per cent. mercuric chloride solution, the first formed droplets gradually develop little not very regular cubes; also double pyramids and irregular forms.

Atrophine sulphate. With potassium bromide and bromine at first an egg yolk coloration, but soon crystals, cylinder to roll shaped are thrown out, in H-like to rhombic arrangement.

Quinine hydrochloride. The addition of sulphuric acid to the aqueous solution of a needle of quinine hydrochloride will produce a pronounced fluorescence, which can be readily observed on the glass slide.

Quinine sulphate: The same test as quinine hydrochloride.

Cocaine hydrochloride. The trinitroresorcinol precipitate grows rapidly to mushroom-like forms. With tetranitrito-diamino-cobaltipotassium, prompt formation of bundles of fine, long needles often appearing like hemispheres connected by bridges. The chromic acid and permanganate reactions of the pharmacopœia can also be carried out microchemically.

Cocaine nitrate. As cocaine hydrochloride.

Codeine phosphate. With iodic acid rod or spear-shape crystals, very often in aggregates. With Pfahl's reagent rods, which arrange themselves in rosette and star forms.

Caffeine. Solid caffeine (it is best to use the solid sublimate) gives with mercuric chloride aggregates of colorless rods. With potassium bromide and bromine, yellow prisms, which are often aggregated

in larger units. The murexide reaction, which the pharmacopœia specifies, can be carried out with 1/20 mgm.

Caffeine Sodium Benzoate. For the caffeine reactions, the residue, which is left by the quantitative determination can be used, but we can also use the caffeine sodium benzoate directly for the reaction with mercuric chloride (sodium benzoate negative). The reactions mentioned in the pharmacopœia with hydrochloric acid and ferric chloride can be carried out microchemically.

Test for sodium, see theobromine sodium salicylate.

Caffeine sodium salicylate. Test for caffeine just as with caffeine sodium benzoate; test for sodium and salicylic acid as in theobromine sodium solicylate.

Colchicine. Colchicine is one of the few alkaloids for which a microchemical crystal precipitation is not known. Of the three identity reactions, which the pharmacopœia specifies, one is sufficient (heating with hydrochloric acid and ferric chloride and extracting with chloroform).

Whether it is possible to smell the chloroform, if the test is carried out with 0.2 gm. of colchicine, is rather doubtful. However, if the smallest particle is added to a little sodium hydroxide and heated with a little aniline, colchicine can easily be identified by means of the isonitrile reaction.

Cotarnine hydrochloride. This salt gives needle and spear-shaped crystals with many reagents, *e. g.*, mercuric chloride, potassium iodide, anthroquinone-sulphonic acid, also with Erdmann's reagent.* Characteristic needles arranged in feather or bouquet shape are produced by Rosenheim & Koppel's reagent.** Sodium perchlorate gives groups of needles in bush or mushroom forms. With sodium hydroxide, an amorphous turbidity appears, with sometimes skeleton forms. Ammonia gives nothing.

Diacetylmorphine hydrochloride. If a minute amount of diacetylmorphine hydrochloride is placed in a solution of mercuric chloride (1:20) the crystals of the diacetylmorphine are transformed into aggregates of fine needles. With potassium bromide and potassium iodide only drops are formed, which with potassium bromide go eas-

*$K(NH_3)_2(NO_2)_4Co$. See *J. prakt. Chem.* [2], 1881, **23**, 249, footnote; also Werner, *Zeits. anorg. Chem.*, 1897, **15**, 165.

$Na_3Co(NO_2)_6$. See *Zeits. anorg. Chem.*, 1898, **17, 43.

ily into solution (difference from related alkaloids). For test for morphine, see ethylmorphine hydrochloride.

Emetine hydrochloride. If a needle of emetine hydrochloride is placed in a solution of anthraquinone beta monosulfonic acid, needles are formed in a bubble-like arrangement.

Dihydroxycodeine hydrochloride. With potassium bromide or potassium iodide needles, spears and rods. If a tiny grain of eucodal is placed into a solution of Erdmann's reagent (see above), rods are formed around the small grains. With iodic acid neither free iodine is eliminated nor a precipitate formed (distinction from morphine and codein). With ammonia a precipitation of various crystals is formed, (prisms, plates, leaflets), which possess a plume-like curved or stair-like margin.

Homatropine hydrobromide. With potassium bromide and bromine a similar reaction to atropine. If crystals of Rosenheim & Koppel's reagent (see above) are added, rods and prisms are formed; with anthraquinone beta monosulfonic acid aggregates of needles are formed. With ammonia turbidity, which disappears on stirring. The turbidity which is formed on the addition of sodium hydroxide can easily be transformed in fine needles and mushroom-like bodies.

Hydrastine Hydrochloride. If a small grain of hydrastine hydrochloride is placed in a solution of Erdmann's reagent (see above), an enormous amount of manifold branched needles, partly curved, are formed. With hexanitro cobalti sodium, spherical crystals were formed, on which developed small needle rosettes or large aggregates of fine slender threads. With potassium iodide, rods, spears, and plates are formed; with mercuric chloride aggregates of needles and spears, often with a saw-like margin, less often of rhombic shape. With sodium perchlorate, crystals are formed, that grow to spears, plates, etc., often with curved margins. With sodium hydroxide, at first turbidity, later needles, spears, etc.; with ammonium hydroxide, nothing.

Lobeline hydrochloride. Of the many precipitates which can be obtained with lobeline hydrochloride and the usual precipitating agents, nearly all are amorphous and not characteristic. An exception is the precipitate with sodium nitrate. At first droplets are formed, but they pass easily into threads arranged as a roll.

Morphine hydrochloride. With mercuric chloride and potassium bromide a deep-brown turbidity obtains, of which fine rosettes and

brush-like bodies are often formed. With iodic acid iodine is liberated (detected with starch) with potassium iodide and potassium bromide, needles, the first one often in rosette form. The aqueous solution will give with sodium hydroxide a turbidity, which on stirring disappears. With ammonium hydroxide gradually rhombic prisms are formed. With ammonium thiocyanate no precipitation was obtained (distinction from related alkaloids; also from apomorphine).

Narcophine. With iron alum, red color; with solution of silver nitrate containing nitric acid, a precipitate (both reactions of the meconic acid).

With sodium acetate and sodium salicylate, precipitates that are transformed into crystals mostly in aggregates (reaction for narcotin). With iodic acid iodine is liberated (see morphine). The crystal line precipitation of the morphine is disturbed by the presence of other substances, except that with potassium bromide crystal formation gradually occurs, partly in form of spherical crystals and rosettes.

Novocaine hydrochloride. With trinitroresorcinol at first granules, then minute crystals becoming aggregates of long needles in clusters and sheaves; rarely small prisms. With Erdmann's salt (see above) groups of needles and more or less long needles. With Reinecke's salt (see special article on this reagent) leaf-like or blunt-ended crystals in rosettes or dendritic forms. The diazo-reaction can be applied. The precipitate with ammonia dissolves in excess.

Novocaine nitrate. Same as the hydrochloride.

Papaverine hydrochloride. Ammonium hydroxide causes a precipitate in the aqueous solution, of which gradually rosettes, bushes or aggregates of needles or rods not uncharacteristic, are formed. All other precipitating agents tried gave amorphous precipitates.

Physostigmine salicylate and sulphate. Microchemical crystalline precipitation, that would have practical value, is not known for physostigmine. However, color reactions can be carried out microchemically. Iodic acid will give slowly in the cold, quicker on heating, a purplish blue (not due to the presence of free iodine). The precipitate obtained with ammonium hydroxide is soluble in excess.

Pilocarpine hydrochloride. With Erdmann's reagent (see above) square plates, and long prisms, appear also saw-like formations. With Reinecke's salt, bush-like formation of branched needles or threads. The precipitate which is formed with copper lead nitrite is trans-

formed quickly into green aggregates, the separate members of which have a round border or form well formed plates and prisms. With trinitroresorcinol, aggregates of needles and spears or long crystals are obtained. With ammonium hydroxide no crystalline formation occurs.

Scopolamine hydrobromide. With Erdmann's reagent (see above), needles, then prisms and rods appear. With anthraquinone beta monosulphonic acid mostly aggregates of needles and spears. With potassium bromide and bromine, according to Eder, yellow amorphous droplets, which grow very often to irregularly shaped, skeleton shaped leaflets and needles. With Reinecke's salt (see special article on this reagent) slow formation of rosettes of small blunt spears, soluble in ammonia.

Strychnine nitrate. Strychnine salts give with all precipitating agents crystalline precipitates, even with salts such as potassium bromide, potassium iodide, ammonium thio cyanate, also with iodic acid, sodium perchlorate, mercuric chloride, also with Erdmann's reagent and that of Rosenheim & Koppel (see above, for these). In most cases needles or aggregates of needles are formed. Mercuric chloride gives rosettes and very finely branched forms, that consist of tiny needles. Ammonia forms needles immediately.

Suprarenin. The usual precipitating agents fail in a solution of 1:1000. Most characteristic is the reaction with mercuric acetate, which at first gives a red coloration, but soon a formation of small grains, and finally aggregates of fine needles, (mercurous acetate?). The reducing reactions with Nessler reagent and ammoniacal silver nitrate give at first red precipitate are obtained with one droplet of the solution (1:1000).

Theobromine sodium salicylate. The addition of a small amount of acetic acid to the aqueous solution, causes the formation of small grains of theobromine and aggregates of crystals of salicylic acid. The latter can be demonstrated in the most minute traces with ferric chloride. On the addition of mercuric chloride (1:20) to the aqueous solution numerous rosettes and stars are formed of theobromine-mercuric chloride. A little of the theobromine-sodium salicylate is ashed on a glass cover; the ash is dissolved in a little dilute acetic acid, the liquid allowed to evaporate in a moderately warm place.

**This Journal,* 1929, p. 724.

If the residue is treated with uranyl acetate, the tetrahedrons of sodium uranyl acetate are obtained (test for sodium).

Theophylline. If to the aqueous solution of a small amount of theophylline, a few grains of mercuric acetate are added, aggregates of needles of mercury theophylline are obtained. If one gives to the solution in hydrochloric acid, potassium bromide and bromine, are added, and the liquid immediately covered with a watch-glass, beautiful bushes and aggregates of needles and leaflets are obtained, which appear mascroscopically as a golden layer.

Veratrine. No reliable microchemical crystalline precipitations are known for veratrine. However, the color reactions are very sensitive. For instance the sulphuric acid reaction will give with the smallest particle of veratrine on the glass slide a green fluorescence as well as a red coloration.

I do not doubt that any one, who uses these tests will find their superiority absolutely established, and that this publication will aid microchemistry to find new friends in pharmaceutic circles. I am quite convinced that microchemistry will find its way into the German Pharmacopœia.

ABSTRACTED AND REPRINTED ARTICLES

OBESITY REMEDIES*

REDUCING remedies in the form of bath salts, foam baths, chewing gums, soaps, creams, pills, wafers, and tablets have been extensively advertised during recent times. Some of these preparations are for external application, while others are to be taken internally, but in all instances they are often represented as "safe, harmless, and efficient" remedies which require no arduous exercise and no starvation diet.

To furnish publishers with basic information on the treatment of obesity the National Better Business Bureau consulted with a number of obesity specialists. We submit below a digest of the information obtained from the authorities consulted.

*Reprinted from *The Long Island Medical Journal.*

Is Obesity a Condition for Which Treatment Can Be Scientifically Prescribed Without a Personal Examination by a Physician?

Treatment for obesity can *not* be scientifically and safely prescribed without a personal examination of the patient by a competent physician. It is essential that the cause of the excess deposit of fat be determined in order that suitable treatment may be prescribed.

There are two distinct groups of overweight persons:

First, there are those who eat more food than they need and who are not sufficiently active to use up this surplus fat through exercise. This group constitutes the greater number of overweight persons. The safe and sane method of control under such conditions consists of diet and exercise. The second group is composed of those suffering from glandular obesity. Each case requires individual study and intelligent diagnosis and treatment. Reducing remedies may be administered by physicians, but only after careful diagnosis and under personal observation and supervision.

It is conceded that persons who are definitely overeating and are gaining in weight due to such overeating could with a reasonable degree of safety reduce their own diet without personal examination or supervision of a physician. Experts point out, however, that it is very desirable for any reduction in diet to be made rationally in order to insure proper balance. A dietitian can advise a diet that will be low in fat-making material, or a dietitian can advise a diet that will be low in fat-making material, or a dietitian can arrange a combintion of foods which will be nutritious and not have tendencies toward the deposit of excess fat, but only a competent physician can determine what is technically wrong with the human anatomy as regards this disturbed functioning and depositing of excess fat or its safe reduction.

Is Obesity a Condition Which Can Be Safely and Scientifically Treated Without the Careful Supervision of a Physician?

Obesity can be neither safely nor scientifically treated except under the supervision of a person with an intimate knowledge of the human body and its processes—that is, a physician.

Here again, a person who is definitely overeating can reduce his own diet with reasonable safety, but it is important that the re-

duction be made rationally in order to insure a balanced diet. Under any reducing regime, secondary disease conditions may arise, which, if unrecognized, may lead to permanent disability, or even death.

Should a Person Undergoing Treatment for Obesity Be Examined Periodically by a Physician?

Periodical examinations by a physician are recommended because it is desirable that the patient's condition be carefully watched. The treatment of obesity is not simple. In difficult cases various problems arise which can be met in no other way except through periodical examinations. Some treatments for obesity carry with them a definite risk to the heart and kidneys and these organs need careful watching. We are advised that a number of obese persons have diabetes often unsuspected by them. It is also possible for the beginning of tuberculosis of the lungs to exist in a fat person and to be aggravated by reducing treatment. The diet also must provide certain essential materials during the period of reducing and the medical examiner must know whether the health is endangered by lack of these and general under-nutrition.

Are Exercise and Diet Necessary for a Safe and Scientific Treatment of Obesity?

The treatment of obesity is primarily dependent upon diet and exercise. Most cases of obesity arise from eating of more food than is actually consumed, the surplus being stored as fat. The removal of this surplus can be accomplished only by reducing the intake or increasing the consumption. These measures are synonymous with diet and exercise, which, therefore, are indispensable.

Each case of obesity is a law unto itself. The amount of exercise and the amount of diet can be scientifically determined only on the basis of an intimate and expert knowledge of the individual under treatment.

Do External Remedies, Such as Foam Baths, Bath Salts, Soaps, Creams, Etc., Have Any Merit as a Fat-Reducing Agent?

Medical experts state that soaps, creams, bath salts and other external applications can have no possible influence in permanently reducing obesity. There is nothing that, put in the bath water, will reduce weight. Hot baths in themselves have some weight-reducing

power because they speed up metabolism, and cause a reduction of weight by sweating out water from the body, but this weight is quickly replaced unless the diet is reduced, so that the actual weight remains unchanged. The addition of foreign substance to the bath water is wholly without any scientific basis. Rubbing and massaging will reduce weight to a limited degree, but any creams or pastes that are used in this treatment serve only as lubricants and do not have any weight-reducing qualities in themselves.

Are Laxative Tablets Effective as Home Treatment for Obesity?

The use of laxatives as a treatment for obesity is considered unscientific. Laxatives may create an apparent reduction of weight to such an extent as they hurry the food through the intestinal tract before it can be properly assimilated.

Instead of over-stimulating the intestinal tract unnaturally for the purpose of hurrying food through before it can be wholly utilized it is obviously more rational to eat less food and digest that which is eaten.

The Use of Tablets Containing Desiccated Thyroid for Home Treatment

The use of desiccated thyroid as a home treatment for obesity is fraught with danger. So powerful a substance as thyroid has no place in the legitimate field of home remedies. Medical experts state that thyroid preparations are a valuable adjunct to the treatment of obesity in the particular cases where the patient is suffering from thyroid deficiency, but they would use it only after careful diagnosis and under their personal observation and supervision.

The majority of fat people do not suffer from an under-active thyroid gland and the indiscriminate sale of remedies containing this product for self-medication is contrary to the public interest.

Summary

The information secured by the bureau on the subject of obesity remedies justifies the following conclusions:

1. Safe and scientific treatment of obesity requires a physical examination by a physician.

2. Safe and scientific treatment of obesity requires careful supervision of a physician during treatment.

3. Safe and scientific treatment of obesity requires periodical physical examination by a physician during treatment to safeguard the health of the patient.

4. Exercise and diet are fundamental in the treatment of obesity but neither exercise nor diet can be safely prescribed without an examination by a physician both before and during treatment.

5. External remedies for use in hot baths are without scientific basis.

6. Rubbing and massaging will reduce the outer layer of fat to a limited degree, but the lubricants used in the process possess no fat-reducing properties.

7. The use of laxative tablets as a home treatment for obesity is unscientific.

8. The use of desiccated thyroid as a home treatment is dangerous to health and contrary to the public interest.

SOLID SPIRITUOUS PREPARATIONS*

By Herbert Skinner Ph. C.

President of the Pharmaceutical Society of Great Britain, 1927-29

SOLIDIFIED alcohol has not the sale in these shingling days which it had when curling tongs and fringes were the fashion, but there is no reason why it should not be more in request than it is. Some preparations show the characteristics of easily reaching a boom sale on account of novelty, and then, equally quickly, sales almost vanish through want of exploitation. Alcoholic preparations for external application are highly valued by the public, and the ease with which they can be supplied in a solid form leaves one guessing why such obvious advantages have been so consistently slurred over. It may be that the method of manufacture was wrong; and in looking up formulas like that recommended in the American Formulary I think this must be the explanation. It reads:

Heat the liter of alcohol in a flask of double the capacity on the water bath to 60 deg. Cent., and then mix with 20 to 30 grams of

*Reprinted from *Canadian Druggist.*

well-dried, rasped Venetian soap and two grams of gum lac. After repeated shaking complete solution will take place. This is put, while still warm, into suitable metallic vessels.

The very thought of having to do this to make a solid linimentum belladonnæ would certainly put me off doing it.

The question of price of alcohol is not one that need be discussed here, since the principles of solidifying is common to them all. I was requested to supply a solid eau de Cologne, which is a little different from a so-called frozen one. Again I sought through the records for a formula, and this is what met me in every reference book:

Melt 4.5 parts of stearin, then add 0.5 of sodium carbonate to saponify and 95 parts of eau de Cologne and heat for an hour in an autoclave; coloring may be added if required. When nearly cold the compound is poured into glass moulds and allowed to set.

I confess I could find no variation from the principle there laid down. The solid alcohol market was evidently a very narrow one, and then came an insistent demand for solid iodine, stimulated, no doubt, by advertisement. At first, the immediate requisite was a preparation similar to the non-staining ones which could be rubbed into the joints without the natural unpleasantness of the denigrescent type. Several formulas were given in *The Script*, built on investigations of mine some thirty years ago for *The Journal of Dermatology,* and subsequently republished in *Pharmaceutical Formulas.* The time arrived when the position of solid alcohol preparations should be on a more satisfactory basis, and as the demand was increasing the work had to be done. The formulas mentioned are, in my opinion, wrong and unnecessarily troublesome. The basic element of solid alcohol preparations is sodium stearate, and the amoun required is 5 per cent. That being so, it was obvious that no time should be wasted in trying to make a stearate extemporaneously when I could buy the powdered stearate ready-made. The method of preparation is a simple one: Triturate the stearate with alcohol into a smooth paste and add at least 50 cc.; warm in a suitable flask plugged with cotton-wool until dissolved, add the remainder and pour into suitable moulds. It sets in a few minutes. Such is the simple solid or burning alcohol ready for use in the orthodox way.

The idea underlying the use of alcohol on the skin is not dehydration but stimulation. Those who want the stimulation on the skin after a round of golf swear that it is a fitting climax to win

and a comfort if the game is lost. I have tried several, and find most of them the source of additional labor and no advantage. After strenuous effort a shower bath and a rub down in a dry climate like that of America in summer-time is for me quite enough. A solidified alcohol preparation would never appeal in a dry country, as it is fluid, and plenty of it is wanted; but a patient in bed with almost continuous pressure on some part would be much better relieved with a preparation based on the underlying principle:

Refined talcum powder	10.0
Sodium stearate	5.0
Orange-flower water (triple)	15.0
Alcohol	to 100.0

Treat the sodium stearate with the alcohol as set out above, and rub the talcum powder into a paste with the orange-flower water. When the solution of stearate is ready, stir in the creamy powder and pour into suitable moulds to solidify.

It might be an advantage to add up to 25 per cent. of talcum powder, and if there are any who still believe in castor oil for this purpose, probably the Board of Customs and Excise might pass it for preparing with industrial alcohol. If we try to think of solid eau de Cologne, or it may be lavender water, or any similar spirituous preparation, isopropyl alcohol proves itself very useful. Made in the fluid form with this alcohol preparations are not quite satisfactory; but if solidified I notice the drawbacks are largely removed. A good formula is as follows:

Ol. bergamot	drs.	2
Ol. limonis	dr.	1
Ol. neroli	m.	20
Ol. rosmarini	m.	20
Ol. origani	m.	6
Alcohol isopropyl	ozs.	20
Aq. flor. aurant. trip	oz.	1

What I would do with this is to use synthetics where possible, increase the origanum to m. 10, and if a cooling effect is desired add menthol gr. 10. The method of preparation is to triturate the stearate into a paste with 10 per cent. of water, add the spirit, plug the container, dissolve with heat, add the oils and then pour into moulds.

In these days of silk stockings (real, artificial, or mercerized cotton) ladies suffer frequently from midge bites; and a formula was given in the C. & D. for an anti-midge preparation consisting of citronella oil and spike lavender. A satisfactory solid one can be made as follows:

Ol. citronellæ	5.0
Ol. lavand. spicatæ	15.0
Sodii stearatis	5.0
Alcohol ad	100.0

The usual method is adopted, and the oils are added after solution is effected. As to iodine, the advantage of a solid form cannot be denied for all uses, save sterilizing the skin. The method of preparation is simple, and follows the routine given:

Sodium stearate	5.0
Tincture of iodine to	100.0

MEDICAL AND PHARMACEUTICAL NOTES

ACETONEDICARBOXYLIC ACID, A NEW BAKING POWDER—A baking powder which does not leave a residue in the finished bread or cake has just been worked out in the chemistry laboratories at the University of Wisconsin, by Edwin O. Wiig. This new leavening agent has as its active agent acetonedicarboxylic acid, which during the baking process disappears entirely as gases.

The formation of carbon dioxide, the gas which "raises" the cake, is only part of the story of baking powder. The other part concerns the product which remains in the cake as a residue. The various commercial baking powders on the market at present leave as residues saline cathartics, such as sodium tartrate, Rochelle salt, disodium phosphate, sodium sulfate or aluminum hydroxide. There is still a question as to the possible ill effect of some of these materials upon health. Hence the advantage of a baking powder which leaves no residue whatsoever. Acetone is the only other substance

formed besides carbon dioxide, and the acetone completely evaporates at baking temperatures.

The new powder depends for its action on combination with the water of the dough, just as do the present powders. Hence in order to protect it from atmospheric moisture it is mixed with starch. This cornstarch has a second function, more important than that just mentioned. Starch makes it possible for the chemist to standardize his product. All baking powders must have approximately the same "raising" strength to make possible the use of any recipe. The housewife-consumer will not consult the label of her tin of baking powder, and then compute whether the "two tsps. b. p." of her recipe should be doubled or halved. Starch takes care of any variation in the amount of carbon dioxide given off by active agents of differing compositions.—*Science Service.*

Sweeter Than Saccharin—A new sweetening compound which is somewhat sweeter than saccharin and 690 times sweeter than sugar has been prepared by Dr. Henry Gilman and J. B. Dickey of the department of organic chemistry at Iowa State College here, from waste products of corn. The name of this compound is "the syn-isomer of 5-benzyl-2-furfuraldoxime."

Despite its sparing solubility in water it may become a pattern for new and valuable sweetening compounds. As yet, no study has been made of its physiological action. It is interesting to note that unlike other artificial compounds of high sweetening power this compound can be readily prepared from sugar by standard organic reactions. Other raw materials, like paper and cellulosic compounds, in general, can be used as a starting point in its synthesis.

Previously, Dr. Gilman and A. P. Hewlett prepared a compound from corn cobs which was 200 times sweeter than sugar.—*Science Service.*

Food Standards Approved—The Secretary of the U. S. Department of Agriculture on November 25 approved the definitions and standards for coffee, milk, and mayonnaise revised and amended by the Food Standards Committee at its October meeting. These revised definitions and standards, given below, are now official for

use in the enforcement of the Federal Food and Drugs Act, which is in charge of the Food, Drug and Insecticide Administration of the Department of Agriculture.

MILK is the whole, fresh, clean lacteal secretion obtained by the complete milking of one or more healthy cows, excluding that obtained within 15 days before and 5 days after calving, or such longer period as may be necessary to render the milk practically colostrum free. The name "milk" unqualified means cow's milk.

GOAT'S MILK AND EWE'S MILK are the whole, fresh, clean lacteal secretions free from colostrum, obtained by the complete milking of the healthy animals, and conform in name to the species of animal from which they are obtained.

SKIM-MILK, SKIMMED MILK, is that portion of milk which remains after removal of the cream in whole or in part.

PASTEURIZED MILK is milk every particle of which has been subjected to a temperature not lower than 142 degrees F. for not less than 30 minutes, and then promptly cooled to 50 degrees F. or lower.

COFFEE is the seed of cultivated varieties of Coffea arabica, C. liberica, and C. robusta. (a) Green coffee, raw coffee, unroasted coffee, is coffee freed from all but a small portion of its spermoderm and conforms in variety and in place of production to the name it bears. (b) Roasted coffee, "coffee," is properly cleaned green coffee which by the action of heat (roasting)) has become brown and has developed its characteristic aroma.

MAYONNAISE, MAYONNAISE DRESSING, MAYONNAISE SALAD DRESSING, is the clean, sound, semisolid emulsion of edible vegetable oil, egg yolk or whole egg, a vinegar and/or lemon juice, seasoned with one or more of the following: salt, sugar, spice commonly used in its preparation. The finished product contains not less than 50 per cent. of edible vegetable oil, and the sum of the percentages of oil and egg yolk is not less than 78.

The Secretary of Agriculture also approved the recommendation of the committee that the present definition of ice cream be deleted. The committee's reasons were that the present definition is not enforceable in interstate commerce because the subject has been specifically covered by laws in the various States and that the definition does not represent modern commercial practice in the manufacture of ice cream.

STERILIZATION OF SOLUTIONS—Details are given of the methods of sterilizing a number of solutions which are employed for injection. The following may be specially mentioned:

Preparation.	Process.	Remarks.
Acoin	Aseptic preparation.	Must be freshly prepared.
Adrenalin	Aseptic preparation in hard glass vessels in diffused daylight or artificial light.	Air-free water to be used. The atmosphere must be free from ammonia.
Alypin	Add to boiled water, heat one minute over small flame.	Must be freshly prepared.
Apomorphine hydrochloride	Aseptic preparation with N/500-HCl.	Stability bad—green-color not permissible.
Atropine sulphate	Steam at 100° thirty minutes or aseptic preparation.	At 100° 0.6 per cent. decomposition occurs; 0.1 per cent. solution must be colorless.
Cardiazol	Steam at 102° forty-five minutes.	——
Choline hydrochloride	Stock ampules of 0.6 gm. diluted with 240 cc. of isotonic salt solution, and very slowly injected intravenously.	Ampules smelling of trimetylamine should not be used.
Cotarnine hydrochloride	Aseptic preparation.	——
Dionine	Steam at 115°.	Must be neutral and colorless.
Diuretin	One hour, and again one hour, finally half-hour at 96°.	——
Emetine hydrochloride	Aseptic preparation.	——
Ergotin	Tyndallize at 80° for one hour on three days.	——
Ext. ergot	Tyndallize at 100° for one hour on three days.	——
Gelatin	Boil solution five minutes, make alkaline with soda, steam on three days at 100° for twenty minutes, keeping at 37° in the intervals.	——
Heroine hydrochloride	Aseptic preparation.	Stability limited.
Homatropine hydrobromide	Aseptic preparation.	——
Hyoscine hydrobromide	Aseptic preparation.	Cannot be kept long.
Iron cacodylate	Aseptic preparation.	——

Preparation.	Process.	Remarks.
Lactose	50 gm. dissolved in 50 gm. of water, and precipitated with alcohol; after standing twelve hours pour off, dry in vacuo, and then aseptic preparation.	——
Luminal-sodium	Aseptic preparation.	To be freshly prepared.
Methylene blue	Steam at 115° fifteen minutes.	——
Narcotine sulphate ...	Aseptic preparation. Double ampule.	——
Novocaine	Steam at 100° thirty minutes.	——
Phenolsulphonephthalein	Steam at 100° thirty minutes.	——
Physostigmine sulphate or salicylate..	Aseptic preparation.	Limited stability. Must not be kept in stock.
Quinine urethane dihydrochloride	Aseptic preparation or tyndallize 70-80° for one hour on three days.	25 per cent. solution must be colorless and free from ammonia.
Sodium arsanilate ...	Aseptic preparation.	Must be colorless and neutral. Do not heat over 80°.
Sodium bicarbonate ..	Aseptic preparation.	——
Sodium cacodylate ...	Aseptic preparation or steam at 110° fifteen minutes.	Must be odorless.
Sodium glycocholate..	Steam at 110° thirty minutes.	Should always be made fresh.
Sodium glycerophosphate	Steam at 115° twenty minutes.	——
Sodium nucleinate ...	Steam at 100° forty-five to fifty minutes on three days.	——
Strophantin	At 90° for twenty minutes on three days.	——
Strychnine sulphate ..	100° for one hour on three days.	Should show no separation of crystals.
Trypaflavine	Steam at 110° for thirty minutes.	——
Yohimbine hydrochloride	Boiling sterile water—no further heating.	Keeps about one week.

Rapp. (*Pharm. Ztg.*, 1929, 74, 678.)—(Through *Quart. Jour. of Pharm.*)

ETHER, ANÆSTHETIC, PRESERVATION OF. C. Langton Hewer. (*Lancet*, 1929, 216, 770.)—It is well known that, when stored,

anæsthetic ether tends to oxidise with the formation of peroxides, aldehydes, etc. Some of the decomposition products are known to be toxic. Several anti-catalysts have been tried, but it has been found

Time of Bubbling $N_2O + O_2$ in minutes	Ether Peroxide (parts per million) Without Copper	With Copper
Nil (control)	Less than 0.05	
Thirty	2.5	1.2
Sixty	2.2	0.2
Ninety	1.0	0.5
Nil (control)	Aldehyde (parts per million)	
Thirty	9.5	2.5
Sixty	11.5	2.5
Ninety	4.0	1.5

that ether stored in copper cans shows no tendency to decompose even in the most adverse circumstances. The author placed a polished copper plate about 8 cm. long and 3 cm. wide in a standard ether bottle of a Boyle's apparatus. One-third of the copper was above the ether level, and nitrous oxide and oxygen in the proportion of 5 to 1 were bubbled through for varying periods. The ether bottle was surrounded by a jacket containing water at room temperature and exposed to a strong artificial light. Above are the results of the analyses.

The author concludes that pure ether treated with carbon dioxide and stored in copper containers will remain pure almost indefinitely, and that if anæsthetic gases are bubbled through ether for prolonged periods the rate of decomposition will be greatly diminished if there is an adequate area of copper above and below the ether level.—E. J. M. (*Quart. Jour. of Pharm.*)

Methyl Alcohol, Test for, in Ethyl Alcohol—H. Matthes. (*Apoth. Ztg.*, 1929, 44, 730.) For the German official test for methyl alcohol it is advantageous to use potassium guaiacol-sulphonate in place of guaiacol, as in practice it is found that there is a possibility of error with the latter owing to incomplete solution of the guaiacol in the sulphuric acid. If the salt contains traces of

guaiacol, a red colour may be obtained in the reaction even in the absence of methyl alcohol, and it therefore should always be purified by dissolving in water and evaporating to dryness. After such treatment, potassium guaiacol-sulphonate gives no trace of red colour when strewn on a formaldehyde-free mixture of acetaldehyde and sulphuric acid, but in presence of formaldehyde the violet colour—incorrectly characterised by the Pharmacopœia as "rose-red"—comes up very well.—G. M. (*through Quart. Jour. of Pharm.*).

PYRETHRUM EXTRACTS—Methyl, ethyl, isopropyl, normal butyl, secondary butyl, and tertiary butyl alcohols, as well as benzene, xylene, carbon tetrachloride, chloroform, ethylene dichloride, amylene dichloride, tetrachloroethylene, and diethyl carbonate, completely remove from pyrethrum the insecticidal principles effective against the aphid *Myzus persicae* Sulz.

Normal and secondary butyl alcohols at 10 per cent. concentrations in water and benzene, carbon tetrachloride, ethylene dichloride, tetrachloroethylene, and diethyl carbonate at 5 per cent. concentrations in ethyl alcohol kill 50 per cent. or more of these aphids without injury to cabbage.

At 5 per cent. concentrations all the extracts except xylene and amylene dichloride give effective control against *Myzus persicae* Sulz. without injury to cabbage.

Normal and secondary butyl alcohols show markedly greater toxicity to these aphids than tertiary butyl and isopropyl alcohols, which, in turn, show markedly greater toxicity than methyl and ethyl alcohols. Roark and Cotton found the butyl alcohols and isopropyl alcohol to be more toxic than methyl and ethyl alcohols, in the vapor phase, to rice weevils.

If cost is taken into account, denatured ethyl alcohol appears to be the best of the solvents tried for extracting pyrethrum when the extract is to be diluted with water for application upon plants.

There is no advantage in the extraction of pyrethrum with these solvents at their boiling point temperatures over that at room temperature.—*Jour. Ind. and Eng. Chem.*, 1929, p. 1253.

BARIUM SULPHATE IN X-RAY DIAGNOSIS—The value of barium sulphate as an opaque medium in X-ray diagnosis depends very much on its physical properties. Preparations of high specific gravity settle down rapidly in aqueous suspensions, and are therefore unsuitable. The German Pharmacopœia, VI., prescribes the following physical test:—5 gms. finely sifted $BaSO_4$ are placed in a graduated glass stoppered cylinder of 50 cc. capacity, the scale of which measures 14 cm. Water is added up to the 50 cc. mark, the whole is shaken for one minute, and then set aside. The suspended $BaSO_4$ must not sink below the 15 cc. mark within a quarter of an hour. A good $BaSO_4$ answering all requirements is obtained by running a filtered solution of $BaCl_2$ of 15° Ré (prepared from witherite, the natural $BaCO_3$, and HCl) in a thin stream while stirring into an excess of magnesium sulphite solution of about 10° Ré. For 100 parts of witherite 110 parts of crude As-free HCl of 20/21° Ré are required, and for precipitation of $BaSO_4$ 130 parts $MgSO_4.7H_2O$; or 70 parts of its anhydrous form, the mineral kieserite, the use of which is indicated for reasons of economy. A specially light product results, if to about 300 litres of the $MgSO_4$ solution a strained decoction of 1 kilo carrageen (Irish moss) is added. Carrageen mucilage has proved a good protective colloid which can with advantage be employed, where very fine light precipitates of insoluble metal compounds are desired. In order to keep $BaSO_4$ better in suspension the addition of gelatin, agar-agar, tragacanth, and mucilage prepared from *Cetraria islandica, Chondrus crispus,* and *Gigartina mamilosa* has been tried. The mucilages of the two latter especially are suitable, as they are almost tasteless, whilst that of *Cetraria islandica* possesses a bitter, harsh taste which, however, can be easily disguised. A good X-ray contrast medium may be prepared as follows: 2 kilos of carrageen are boiled for one hour with 60 litres of water, replacing loss by evaporation. The mucilage is then passed through a hair sieve; what remains on the sieve is boiled again, first with 20, then with 10 litres of water, and the three lots of mucilage are united. On the other hand 1.2 kilos of finely powdered tragacanth are carefully mixed with 60 kilos of $BaSO_4$; the mixture must be sifted several times to secure uniformity before it is added to the carrageen mucilage and well worked up with it; then it is dried at a temperature not exceeding 60° C. Rapid drying is essential, as otherwise the product easily acquires an unpleasant smell; if the tem-

perature rises above 60° C. during the drying process, a bitter taste results. The dried mixture is then ground and passed through sieves until the required degree of division has been reached. The product is a fine powder of yellowish-white colour and insipid taste; 32 gms. rubbed down with 60 gms. water of 45° C. forms a smooth cream which, if transferred to a large test-tube, should not separate within two hours. The preparation is principally intended for rectal administration; its taste is too insipid for internal use, but can be improved and made suitable for internal use by certain additions, for instance: to 45 kilos $BaSO_4$ mixture 1.5 kgm. dried milk powder, 3 kgm. cocoa, 10 gms. vanillin, and 10 gms. saccharin are added. As, however, patients with stomach trouble often have an aversion to cocoa and saccharin, other flavorings might be substituted. Inspissated juice of cranberries, prepared by boiling the berries thoroughly with sugar until they form with a little agar-agar a jelly, makes an agreeable vehicle in the proportion of 1 part to 2 parts of the $BaSO_4$ mixture. —R. A. Feldhoff (*Pharm. Ztg.*, 74, 61, 980, *through Pharm. Jour.*).

BOOK REVIEWS

MICROSCOPIC PHARMACOGNOSY. By William Mansfield, A. M., Phar. D., Ph. G., Dean and Professor of Botany and Materia Medica, Union University, Albany College of Pharmacy, Albany, N. Y. 88 pages of descriptive matter, 88 full page plates. Cloth. 5x8; 1929; $3.00. John Wiley & Sons, Inc., N. Y.

This new publication will be a welcome edition and addition to the reference library of any student or laboratory worker interested in the identification or verification of authentic vegetable drugs by their diagnostic or histologic characteristics. The internal structures and cell arrangements of eighty-eight powdered official and unofficial drugs are illustrated with full page cuts and fully described on an opposite page.

The book is arranged according to a morphological classification. Before any group is pictured or described a full page is devoted in naming the drugs of the group, by their official Latin titles and botanical origins.

The morphological groups considered in their order of presentation are as follows: Leaves and leaflets; leaves and flowering tops; flowering plants and herbs; flowers and flower buds; fruits; seeds; corms; bulbs; tuberous roots; barks; woods; rhizomes; rhizomes and roots; fungi; galls; pith and nine unofficial drugs. Representative drugs of each group are pictured and described.

No plant families are mentioned; neither are measurements of individual histological characteristics stated. The drawings are made to scale but magnifications omitted. The descriptive matter is excellently presented.

W. J. S.

THE "WELLCOME" PHOTOGRAPHIC HANDBOOK, 1930. The 1930 edition of the "Wellcome" Photographic Exposure Calculator, Handbook and Diary is a worthy successor to the many previous editions of this popular handbook.

The text has been completely revised and a number of additions made to the exposure tables. This compact handbook, neatly bound and complete with pencil, can be carried easily in the pocket ready for instant reference. The information it gives is the result of many years' practical experience and is equally useful to the expert and the beginner. Excellent examples of the fine quality obtainable in difficult subjects by developing the negatives with "Tabloid" "Rytol" are shown in the frontispiece illustrations "The Woolworth Building, New York" and "T. R. H. the Duke and Duchess of York leaving Holyrood Palace."

Instructions are in simple non-technical language and provide a reliable guide from the moment of exposure to the finished print. The numerous tables, figures and other data will be found invaluable. The memoranda pages provide ample space for personal records of exposure, subjects, stops, etc.

Four editions are issued: Northern Hemisphere and Tropics, Southern Hemisphere and Tropics, Australasia and Tropics and United States of America.

The price in the United States is seventy-five cents per copy. Burroughs Wellcome & Co. (U. S. A.) Inc.

MIKROCHEMIE DER ARZNEIMITTEL UND GIFTE. By Adolf Mayrhofer, Ph. D., Pharm. M. University of Vienna. Part II. 269 pages, illustrations in the text and photogravures of microscope fields, 8vo. Berlin, Urban and Schwarzenberg, 1928. M. 16.

This part of the work is devoted to medicines of organic origin. A careful critic might accuse the title of tautology, since almost all of our really useful drugs are poisons. The object of medication is generally to disturb function, and disturbance of function is practically poisoning. A purge irritates the intestine; a greater irritation might be fatal. An emetic irritates the stomach, tartar emetic is certainly a poison. So we may go through the list including strychnine, morphine, alcohol, mercury and arsenic.

The text of this book is devoted to the recognition of all the important medicines of organic origin by tests in which minute amounts of material may be used. Many accessory compounds not included in the materia medica are also described and their detection indicated. In the early pages much space is given to descriptions of the methods of making tests, including directions as to the use of the miscroscope. Micro-apparatus for distillation, sublimation and other laboratory manipulations are figured and described.

Many photogravures of microscope fields are included, especially in an appendix of plates, but the reviewer cannot give praise to these. They are in the first place unnecessarily large. Selected fields of about two-thirds the diameter would be more satisfactory. A criticism that applies to most books of this character is that the photographs or drawings are made from pure materials and under known and controlled conditions. The research worker or toxicologist encounters organic medicines or poisons (if we make the distinction) in mixture with much other organic matter and often with several substances of the same general nature. Nor does it seem worth while to lay so much stress on the small amounts of the material that may be used. Micro-analysis may be necessary in some cases, but in general, material is cheap and abundant, and convenient quantities may be used. Mineralogists, who are the most intensive students of crystal forms, deprecate strongly the use of such terms as "needles," "brushes," "dendritic forms" as descriptions of microscope fields. In most cases the proper crystallization can be obtained by carrying out the reaction in a small test-tube and transferring some of the precipitate to the slide.

The book contains a very large amount of information expressed in clear language and will be a useful companion for the pharmacologic laboratory.

H. L.

DIE KAKAOBUTTER U. IHRE VERFÄLSCHUNGEN. Dr. H. Fincke. 8vo. 238 pages, 2 illustrations and a table. Wissenschaftliche Verlagsgesellschaft. Stuttgart. M. 20.

This is number 12 of a series devoted to the chemistry of fats. The fact that a volume of this size can be limited on one fat, shows the high specialization of the science. Chocolate products are, however, in most extensive use, many thousands of tons being imported into the leading countries, the United States being, of course, among the largest users. Of the three products which enter into the cups "that cheer but not inebriate," chocolate finds employment in many forms not open to tea and coffee. Linné dubbed it, "food for the gods" but perhaps he was over-enthusiastic.

The volume in hand is devoted to the examination of the chocolate fat, which has many uses and is liable to a variety of adulterations, the book was primarily written in response to a prize offering by the Association of German Chocolate Manufacturers, for the promotion of exact knowledge concerning the whole subject of the commercial and practical relations of the product. In the preparation of the work, the author has put to one side most of the existing literature, and entered upon original investigations. Some alterations and additions were necessary because of the interval between the submission of the mss. and the publication. These have been duly supplied and indicated. The many products of cacao-butter are given full consideration and the author believes that the book represents the latest known data on the subject and will serve as a guide in detecting adulterations for some time. Standard methods of analysis have been fully considered. The investigations have been facilitated by an abundant supply of the material of authentic quality. There is added also a section on the development of standardized methods for edible fats. The book can be earnestly recommended to all who have interest in chocolate in all its relations. The publisher and printer have also done creditable work.

H. L.

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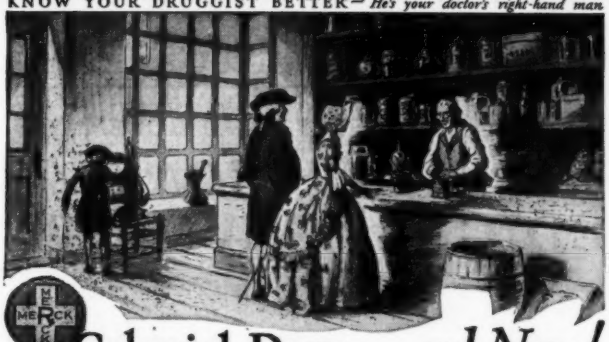

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